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PREVENTIVE
INOCULATION.

—BY—

FRANK S. BILLINGS, M.D.

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PREVENTIVE INOCULATION.[1]

BY FRANK S. BILLINGS.

PREVENTIVE inoculation is an unquestionable possibility in all diseases of a non-recurrent character. Nature has indicated this fact for hundreds of years, but man has scarcely learned to appreciate it. We start upon an already open path. At its very entrance we can see the guide-post "non-recurrent." To pass on to success requires simply honest and heroic workers. The spirit of a common humanity should rule where greed for the almighty dollar now reigns supreme. The nation itself must be educated to an appreciation of what can be done; then success will come. Only heroes can do such work. The present reign of mediocrity and unprincipled selfishness in our laboratories must be crushed. Better anarchy than the existing conditions! Fraud rules in the place of scientific honesty. Salary grabbers occupy places which should be filled by original investigators with the true scientific spirit. No mind but a free one can investigate correctly.

The Difference Between Experimental and Preventive Inoculation.—These two procedures must be most sharply differentiated. While preventive inoculation must necessarily depend upon experimental for its perfection, we have no need to resort to it to demonstrate prophylaxis by this method to be a possible fact. Preventive inoculation does not depend upon experimental for its demonstration as a possibility. Nature has already done that, as mentioned.

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[1] Read before the Section for State Medicine at the Annual Meeting of the American Medical Association, Nashville, Tenn., May 22, 1890; and the Chicago Medical Society, June 2, 1890.

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The True Value of Experimental Inoculation.—What do we mean by experimental inoculation? Let us thoroughly understand that first.

By experimental inoculation we simply mean the transference of the disease products (or, pure cultivations of the micro-organismal cause of a given disease) from diseased to healthy individuals of the same, or other species of animal life, in order to see what the results may be.

It is an attempt at transference, nothing more.

The success of such an experiment is determined entirely by the nutrition offered, by the animals inoculated, to the germs of the disease inoculated.

The amount of imbecile nonsense which has crept into medical literature upon this subject is almost indescribable. Koch and his school are almost entirely to blame for it. It shows an utter want of true pathological knowledge and philosophical acumen. It is entirely wanting in sequential logic.

It has been assumed that experimental inoculation in small animals must of necessity determine the real nature of the disease of the animal from which they were inoculated. Such a hypothesis is absolutely absurd. It need not necessarily determine anything of the kind.

These writers do not know the logical definition of the word *contagious*. While they frequently write deftly about "faculative" and "obligatory parasites," their language in regard to the results of experimental inoculation shows that they use words without knowing their logical application. They speak of the "contagion of anthrax" (a faculative parasitic disease), and the "contagion of glanders" (an obligatory parasitic disease), in the same breath. Logically speaking, the word "contagious" simply means the coming in contact with an infectious principle, utterly regardless of its origin. It may be a syphilitic person in one case, and a filth hole in the ground in another. Both may be equally "contagious," but the inficiens in each case had a different origin. This, and this alone, must decide the nature of a disease. They must, of necessity, be either ex- or endogenous primarily. Practically, all physicians and hygienists know what they mean by a "contagious" disease. They mean that a diseased individual must be, or has been, present of a given species of animal life as its primary source of origin. Historically, we know of no other primary genesis for these diseases. We know that no individual can acquire syphilis, or glanders, or scarlet, or mumps, unless an individual having been afflicted with one of these diseases has been in the immediate vicinity. The closeness of the contact necessarily varies in different diseases. Remove such diseased individuals, clean up or destroy their belongings, and the danger of contagion is removed.

Experimental inoculation cannot strengthen the case in the least degree. The endogenous character of such diseases, that they were strictly contagious in the practical sense, was known centuries before a bacterium was ever heard of. Only bacterio-fanatics seem to be ignorant of this fact. Inoculation of small animals cannot strengthen it an iota. To ignorant minds it might weaken the practical everyday evidence. All animals are not equally susceptible to a given inficiens. Even though experimentally inoculable, a given contagious disease often loses its specific, practical characteristic by inoculation in experimental animals of a given species, but different from that in which it naturally occurs. For instance: glanders, transmitted from a diseased horse to rabbits or guinea-pigs, will not extend, of itself, to uninoculated rabbits or guinea-pigs. It is not contagious in these animals.

A recent writer says that the "crucial test" of the contagiousness of tuberculosis was only obtained when the results of inoculation in rabbits and guinea-pigs had become known. Nonsense! The "crucial test" is the result of contact between diseased and healthy individuals of the species in which a disease naturally occurs, or is naturally transmitted to by accident. According to these absurdly illogical observers of pathological phenomena, syphilis should not be contagious because non-transmissable by inoculation to domestic animals. Why any sane person, looking upon himself as an investigator, especially such an one as Koch, should speak of the contagion of anthrax, swine, plague, diphtheritis, or rabbit septicemia, passes one's comprehension. The latter disease has been especially mentioned, because it is not a natural disease in rabbits, simply to demonstrate the utter absurdity of this position.

The word "contagious" does not properly express the practical and hygienic meaning attached to the diseases to which that name has been given. As repeatedly stated, and as must be definitely understood, it simply means contact with an inficiens, and has no absolutely necessary connection with origin. Let us illustrate this with an example: A physician makes an autopsy on two different people on the same day; the one has perished from syphilis, the other from anthrax. In both cases he accidentally cuts a different finger, and in one becomes a chancre, in the other a malignant pustule develops. Such a thing is possible, but not probable. What has taken place? Accidental inoculation, through contact with two differently-diseased individuals — contagion. The primary origin of these two diseases has been entirely different, however. The syphilis primarily originated from another individual; the anthrax from the ground of some locality. The one is endogenous, the other exogenous. This at once demonstrates the folly of any further use of the word "contagious" in the differential classification of diseases, as it does not express our true meaning.

To sum up, then, we can logically speak of diseases as extra-organismal, or exogenous; intra-organismal, or endogenous, and sporadic—that is, of undemonstrable origin; or, in other words, from the etiological point of view we can logically only classify diseases according to the primary origin of their cause. Or, to speak with Hueppe, as "obligatory parasites," by which he means that such etiological moments are primarily bound on the conditions offered by some form of animal life for their existence and continuous development; or, in other words, such diseases are "endogenous" in origin, to speak with Pettenkofer, or intra-organismal in origin, as I have termed it.

An endogenous disease is one which, so far as we can historically trace its genesis, has found, and still finds, its locus of primary origin for each new outbreak or extension of the disease in a diseased individual of some given species of animal life (and never in any other way), and then passes directly from the diseased individual to another susceptible, healthy one, either by direct contact or cohabitation, or by contact with some effluvia, secretion, or other material which has either come directly from, or been in immediate contact or relation with, such a diseased individual.

Speaking in the old sense, such a disease would be "contagious." Speaking according to the nonsensical usage of the word at present, no one can tell what its true origin might have been.

In contradistinction to obligatory parasitic diseases, Hueppe has given us the term "faculative parasites," by which he means to indicate diseases of parasitic origin, in which the point of primary development of the germs is invariably outside the animal organism; but they have the faculty of living for a time within the organism of certain species of animal life, becoming parasitic or disease-producing for the time, when such animal organisms offer the necessary nutrient conditions to their life. To this class Pettenkofer has given the name "exogenous," while I have termed them "extra-organismal," or diseases which find their primary origin in external or surrounding conditions. Or, in other words:

An exogenous disease is one which invariably finds its locus of primary origin not in, but outside of, an animal organism; that is, in the earth, or in the surroundings of animal life, where its micro-organismal cause develops under certain conditions of climate and soil, which offer the necessary nutrient conditions to the life and continuous development of its germ.

The infected earth or locality bears the same relation to animal life in the origin of exogenous diseases that the infected animal organism does to healthy susceptible animals in endogenous diseases; that is, they each form centers of primary origin regarding specific diseases in their respective class, but with this difference: *the focus of primary generation, or infection, is fixed in exogenous diseases, while it is movable in endogenous.*

The locus infectionis, that is, the point of primary infection or origin, is contagious in either case. In the one, a healthy susceptible individual must come in direct contact—that is, be upon, or in, such an infected locality, or come in contact with material derived directly from such a locality; while in an endogenous disease the same occurrences must take place in reference to some form of animal life. Hence it is to be readily seen that the word "contagious" has no logical use or place in the nosology of diseases, according to the results of modern methods of investigation.

Preventive Inoculation.—Preventive inoculation is an entirely different procedure. It is based upon a natural phenomenon, viz., that a given disease is non-recurrent in character. But more; that this non recurrent condition of the organism is produced equally as well in the mildest attack of a given disease as in cases in which the diseased individual barely escapes with life. Diseases of this non-recurrent character are small-pox, typhus abdominalis (vulgarly called typhoid fever), measles, mumps, scarlet, whooping-cough, chicken-pox, yellow fever, and some others in the human family; and in the domestic animals some of the so-called horse distempers, contagious pleuro-pneumonia in cattle; anthrax, swine-plague, rouget in swine; hen cholera, Southern cattle plague, (Texas fever), and black-leg, and probably the corn-fodder disease, and others.

Some authorities assert that Asiatic cholera is also non-recurrent in character, and I am inclined to think that glanders can be made so by the inoculation of farcy in a mild form. There are probably quite a number of these diseases still unknown to us in the poorly-investigated portions of the globe. I am one of those who, at present, does not believe that rabies is a non-recurrent disease, and hence have no faith in inoculation as a preventive. That non-recurrent diseases can be prevented by inoculation was first discovered in small-pox, and then demonstrated by Pasteur to be possible in anthrax, hen cholera, and rouget, and by Arloing and others in black-leg; by Willems in pleuro-pneumonia in cattle; by Freire in yellow fever in Brazil; by the author in swine-plague, and by Dr. Paquin, of Missouri, in Texas fever in this country. With none of these diseases but small-pox can we claim to have arrived at any perfected

Greenland died—7,000. The deaths from this disease equalled the births at Turin, Italy, from 1796 to 1797. In Prague, Germany, the deaths were 6,686 in 1796, and 15,558 in 1799. In Prussia, 1796, 24,646. In the province of Wurtemberg, in 1790–1800, 36,933. France, from 1726 to 1754, 760,000, of which Condamine says[1] that this number of lives could have been largely saved had there been a general recourse to variolation. In Sweden, from 1749 to 1765, 144,194 deaths from small-pox were reported. In London, in sixty-seven years the deaths from this cause were 113,851; and from 1837 to 1840, 36,000.

Why was variolation resorted to? There must have been some one striking phenomenon in the clinical history of the disease which attracted even the general attention of the common people. What was it? It was the fact that the disease, in general, was "non-recurrent" in character. Outbreaks at that period of the world's history occurred almost constantly, though in some years, or at intervals, to a far more murderous degree than at others. This condition of things soon demonstrated to the people that, as a rule, those who had the disease once seldom suffered a second attack. They had abundant opportunities to test this fact. They also discovered a second fact, which was of far greater importance. They noticed that in years when the disease only appeared here and there among the people, and not as a general epidemic, that it was unusually mild in character; and also, that those catching (contagion) the disease from others generally had the small-pox in the same mild manner. In other words, as in other things in nature, they saw that "like (generally) begat like," or that a mild, a non-malignant type of small-pox in one individual generally produced the same character in another, if exposed to infection from the first. As has been intimated, the Chinese, and other Asiatic people, observed this valuable fact centuries before it received any recognition in Europe. They were then well acquainted with several facts in the history of small-pox, which were:

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[1] Memoire sur l'inoculation de la petite-veriole, 1854.

1. That when malignant in its first appearance, it would preserve that character among the whole population.

2. That when mild it held the same course.

3. That it was non-recurrent, as a rule.

This last was a tremendous discovery. These so-called barbarians seem to have been practical enough to endeavor to take advantage of these phenomena. Knowing the difference in the results between a malignant and mild outbreak, and that the disease did not generally recur again in the same individual, and that at no time could those that had not been diseased be safe from its ravages, they took advantage of the mild outbreaks and tried to induce the disease, at such times, in every susceptible member of the community.

The first attempts at transference were those most natural to occur to the untutored mind—non diseased persons were obliged (or did it themselves) to wrap the clothing of diseased ones about them, or the scabs were rubbed on the skin, or upon scarified or wounded places. In India, where the history of variolation seems to extend into the misty and indefinite past, it was entirely in the hands of the Brahmin priests, and hence, acquired a very wide extension. They had certain seasons of the year in which they went among the people for this purpose, who were especially prepared for it, by certain known dietetic regulations. The priest then went from hut to hut variolating the people at the door. The point of attack was the outside of the fore or upper arm. The skin was washed thoroughly and then rubbed hard with a dry cloth at the point selected, small incisions being made in it. The virus inoculated with was from the previous year and dried on cotton, which had been saturated from diseased individuals. They never used fresh material. Variolated people were subject to especial hygienic rules for a period of four weeks.

It is said that the danger from this treatment was so small that it was rare that any one died therefrom. It seldom failed to give protection. In Circassia it was resorted to in the early life of the maidens, in order to preserve them from the scars of the natural disease which would render them unsuitable for sale to the lords of the harem.

From Asia, Arabia and Northern Africa, this procedure finally extended to Europe, by the way of Turkey and Greece, but found the most bitter opposition from the physicians of the time, and the clergy, the chief objection raised being that it was trifling with the will of God to take measures to prevent anything which He caused; that small-pox was a punishment of the Lord's for the sins of humanity, and hence justly deserved. (See De Hæn and other writers of the period. Hæser, "History of Medicine." Bohn, "Handbuch de Vaccination," and other works upon small-pox).

Early in the seventeenth century, however, variolation became a "boom" (if I may be allowed a modern expression) in England, which was instigated by a courageous woman, Lady Montague, the wife of the British Ambassador at Constantinople, where she had seen the procedure and learned of its real benefits. On her return to London, in 1717, she had her six-year-old son variolated, and four years later, her only daughter. This venturesome act set all fashionable London in a whirl of excitement, and by order of the king, six persons that had been condemned to die, were pardoned on condition that they would subject themselves to inoculation, and then be exposed to small-pox. This was done, with the most positive and satisfactory results. Soon afterwards, the children of George I were inoculated, and then the treatment became more or less fashionable.

It is only justice to the fair sex to mention that, to a woman also, the Marchioness Buffalini, is due the generalization of variolation in Italy.

Variolation had two historical periods. The one, beginning, as has been shown, in the earliest days of historical record, and extending to the year 1760. This may be called the Crude Empirical period.

The second, which may be called the period of Exact Scientific Observation, began and continued to the demonstration of vaccination by Jenner, May 14, 1796.

If vaccination had its Jenner, so had variolation its Gatti, to whom the world is equally indebted, for it was almost entirely due to the acute observational powers and logical conclusions of this great Italian physician, that variolation itself became an almost safe and equally valuable prophylactic measure to vaccination. Though there seems to have been no historical connection between the work of Gatti and Jenner, still the one did prepare the way for the other, for Gatti demonstrated most conclusively the almost safe prophylactic power of variolation (to the individual inoculated), and hence, his work gave a substantial and practical foundation to vaccination.

Variolation was the first great and successful experiment in the history of pathology, as well as the very foundation of preventive inoculation. It was the first practical demonstration of the fact that non-recurrent diseases could be actually prevented by artificial inoculation; that the art of man could successfully reproduce the work of nature; that, as in nature, a mild attack of non-recurrent disease occurred, so could man, by the transmission of the disease-product, from such a person to a healthy individual, also produce the same mild disease; and, hence, induce in the inoculated individual that same immune condition which nature produced, under similar circumstances.

The name of the real European founder of such a beneficient procedure should not have been allowed to have been so profoundly buried in the archives of medical history. How many American physicians ever heard of the name of Gatti, and yet it should be kept as fresh in memory and crowned as plentifully with laurels of gratitude, as that of the ever immortal Jenner?

Regarding Gatti's relation to variolation, I will take the liberty of quoting directly from Bohn, who says: "No one penetrated more profoundly into the essentials of variolation than Gatti, and no other succeeded as well as he. Gatti is a wonderful phenomenon in the history of medicine in the past century. Nearly every page of his little book on variolation astonishes one by its richness in ideas and its advance over those ruling in medicine at the time. He was a thoroughly unprejudiced and positive observer, sharp and logical in conclusions, with à clever understanding of the nature of pathological experimentation, and knew how to give the correct answer to questions coming before him. One can have but a very superficial idea of variolation in the previous century who has not studied Gatti's work, which is characterized by its clear method, modesty and great humanity."

Gatti's instructions as to the treatment of persons to be inoculated, carry us back to our youthful days, when we had to be prepared for vaccination with cooling salts and other restrictive dietetic measures. He says: "All physicians have said that the persons to be inoculated must be, first, prepared; second, such inoculation-traumata must be made as to allow for a free outflow of the inoculated material; third, as soon as the eruption appears, the patient must be treated with all the care and assistance possible to the physician. On the contrary, I say; patients need no preparation; the physician should never provide for the outflow of the inoculated material by such wounds; and the inoculated person should be left to nature." "To prepare an individual for inoculation is the same as endeavoring to give him a certain predisposition which one considers necessary in order that the inoculated disease shall do him the least possible harm. Is there such a disposition, or can such be produced? We do not know it and hence cannot produce it. Health itself is the best condition, and this alone has one to consider in variolation. An unhealthy person must be first made well before he can be inoculated, but those who are healthy are already prepared for it. Every special preparation on the part of the physician is, however, dangerous. Only those things must be avoided which are liable to interfere with the health. All conceptions as to the preparation of the individual, all endeavors to purify or refresh the blood, or to prevent the inclination of the blood to inflammation, no soul in the world understands, and all endeavors in these directions can only lead to the injury of the individual."

Of inoculation he says: "The material with which we will inoculate must be introduced into the vascular layer of the dermis. The variola virus is so intensive that the most infinitesimal amount is as serviceable as a great mass. It is sufficient, therefore, to simply scratch the epidermis with a needle moistened with the virus, or push it gently for a short distance under the same. This way was first introduced by the inoculators, mostly women, in Greece and Italy, and gave most satisfactory results. Only the physicians have sought to replace this simple and efficacious method by more artificial ones and complicated apparatus."

The barbarism of the physicians of the time cannot be overestimated. Extensive incisions were made in the flesh and the cavity filled with thread saturated in the secretion of diseased persons, or even pieces of their filthy clothing placed therein and held in place by bandages. In other cases, a whole skein of thread would be soaked in such secretions and drawn through the flesh, as a seton. The terrible results and unfortunate complication of such methods can be well appreciated at present, and the value of Gatti to the world better understood now than ever. His motto was, " Inoculate cleanly and delicately, and all after treatment is unnecessary." It is a matter of question if that advice is not as applicable to-day as when he wrote, even with our improved methods of obtaining virus. I have seen physicians vaccinating the poorer class of school children, use the same lancet to scarrify the arm on one after the other, with no attention given to washing the arm, that in many cases were dirty enough. To my mind such a procedure is criminal carelessness, and does much to bring vaccination into evil repute and furnish just and apparently reasonable objections to its opponents. It suffices to say that Gatti's success as a variolator was phenomenal, and that his reputation extended all over Europe. So great did his skill in diagnosis become that he could almost invariably select the correct type of the disease from which to produce the same mild form in the persons inoculated. Very few pustules followed his treatment, and only slight constitutional disturbances in most cases. In fact it is due to Gatti alone that variolation became a reasonably safe procedure between the year 1760 and the introduction of vaccination by Jenner.

Objections to Variolation.—Variolation was not only resorted to as a strictly prophylactic measure, but also that the march of the disease might be hastened, and every one in a community, not previously diseased, might have it at the same time. Variolated persons were, however, as dangerous to healthy ones as those acquiring the disease in the natural manner. They had the small-pox, and hence could be the means of extending it. Therefore, while most extensively practiced, and in many cases made obligatory by law, on the outbreak of small-pox in a locality, still such places were treated as pest-centers, and all communication between them and the surrounding world was shut off until the disease was declared at an end, and the locality cleansed and disinfected, as best they knew how.

The cleverness of these early variolators cannot be overestimated. They insisted that persons to be inoculated be kept by themselves, or from general intercourse with the people for twelve to fourteen days previous to the operation, in order to avoid, as far as possible, the danger of natural infection. They discovered that early childhood was the best time to inoculate, and also that the virus mitigated somewhat in virulence when transmitted from individual to individual. They also paid strict attention to using the clear lymph before the eruption became pustulous, and even collected it in fine glass tubes for conservation. The crusts were also pulverized and so preserved. They found that certain persons were immune towards variolation, about five in one hundred, which, singularly corresponded with the per centage of immunity noticed in natural outbreaks of small-pox. It is easily to be seen that, at the best, variolation was a somewhat dangerous procedure; not only could it extend the disease, but fatality sometimes followed it, per centage being about one to one hundred. Nevertheless, it was a vast advance in prophylaxis, as can readily be seen by comparison with the death rate from the natural disease. Then again, it was found very difficult to exert a proper control over all the inoculated persons, as they were frequently scattered through the community, thus making centers of danger wherever they might be. Notwithstanding all this, there is no doubt but what it proved a great blessing to humanity, and was the means of saving thousands of lives and much misery.

While variolation was forbidden on the Continent of Europe, soon after the discovery of vaccination, it was continued in England until the year 1840, and practiced fully as much as vaccination, when it was also forbidden. It is still practiced, however, among many of the people of Asia and Africa.

Jennerism.—The word "vaccination" is derived from the Latin word "vaccina," of, or from, a cow, and expresses the transference of the disease known as the cow pox, "vaccina," from cows to man. There has been much discussion in the past as to the true nature and origin of cow-pox, without any uniformity of opinion having been arrived at. To my mind it seems as if the observers were almost entirely without ordinary powers of reflection and the ability to draw sequential conclusions. Variola, or small-pox, has been given different names, according to the species of animals affected, as V. bovina, equina, ovina, and humana. The fact that the inoculation of an animal of a given species, from one of another species, afflicted with the variola common to it, generally protect the first from either natural infection, or the inoculation of the disease common to its species seem never to have been properly appreciated. To my mind it indicates a common origin, and that there is but one variola.

The two malignant forms are those seen in man and sheep, while in cattle and horses the disease has a benign character. Sheep have been protected against variola by vaccination from cattle, and cattle and human beings by ovination from sheep. In fact, ovination of human beings was once looked upon as fully equivalent, in preventive value, to vaccination.

As has been said, these facts of general prophylactic relations between the various variolas, surely indicate but one original form. Whether that point can ever be distinctly decided may be doubtful, but there is no doubt whatever but what we can at once deny all idiopathic attributes to variola in cattle and horses, and emphatically assert that as diseases sui generis they should have no recognition. In fact, in both cattle and horses, variola fails its one essential characteristic. It is not contagious. Transmission by means of the milkers does not constitute contagion!

The transference, inoculation, of either human or ovine variola to cattle through a continued series of these animals, soon mitigates the virulence, so that when again inoculated upon the original species, the contagious factor has been lost. But this is another most valuable pointer in the direction of the original variola. In the days of variolation the most celebrated observers all agreed that the virus of smallpox itself became mitigated on being transferred from man to man through a large number of generations, or individuals. No such phenomenon as this has ever been observed in sheep-pox. It does not lose in virulence in being passed from sheep to sheep. On the contrary, sheep-pox becomes mitigated by transference in all the animals it has been attempted on, man, cattle, rabbits, goats, and horses, but the contrary experiments have never been essayed. Vaccina has never been carried through sheep for a long series of generations, nor has small-pox, nor the eruption in horses. All this demonstrates one fact, that if every other kind of variola loses in virulence, even by transmission in its own species, (using the accepted idea of specific variola) except that of sheep, then the ovine organism provides the most suitable nutrition for the preservation of virulence alone—contagiosity, the human next, while in cattle and equines it is soon lost altogether.

As a matter of experiment, and great pathological interest, it is important to endeavor to build up vaccina to contagiosity again in sheep, if it can be done. It is singular that observers should have looked upon the bovine and equine complications as idiopathic, when in the former it is limited almost entirely to cows, and in both is not a natural contagious disease, only extending by accidental transmission.

It is a matter of absolute certainty that vaccina either owes its origin to the human or ovine disease, most probably the former; and that it was transmitted to cows in past ages in some way by milkers, who also took care of their friends diseased with small-pox, and then the eruption was transmitted in the same way, by the milkers, from cow to cow in a herd, and in this way the disease acquired a constant degree of mitigation—in fact, absolutely lost its virulence, or contagiousness, but still retained the prophylactic principle. Right here let me make a statement which seems to have escaped notice, or expression, at least, and which is of the utmost importance in the study of preventive inoculation: What does this peculiar deportment of vaccina teach?

The very fact that the virulence, contagiousness, of small-pox having been lost in the change from variola to vaccina, shows us that the germs of non-recurrent diseases have the ability to produce two different chemical materials—one pathogenic, the other prophylactic, and that tests of virulence have no value or control in the question of prevention.

Later on we will return to this question in detail.

It seems never to have been properly appreciated, that there is not on record one single eruption of variola in cattle or horses of a general or epizootic character. As a herd disease, under natural or free conditions, we have no record of it. This again tends to support the hypothesis that the disease in these two species found and finds its origin in the small-pox of man, rather than in the variola of sheep.

Again, as strong proof as can be brought to bear in favor of both these suppositions, and of vaccination itself, is given by the fact that, with the generalization, or compulsion of vaccination, not only has small-pox been brought under most wonderful control, but cow-pox has been almost entirely lost sight of. While there have been cases of small-pox every now and again, and sometimes quite a number in a locality, no one ever hears of a case of cow-pox, and seldom of anything causing a suspicion of the same.

Bohn says, that while vaccination had its Jenner, it was never fortunate enough to have had its Gatti, as did variolation. When I read that passage I could not but think that the worthy German had spoken in ignorance, and that vaccination had indeed had one to take part in its development; one the equal of the great Italian in every respect; one whom we should all delight to honor and to whom this country owes a monument of gratitude, if humanity does to any man, in its development on American soil. I allude to the late Dr. Henry A. Martin, of Boston, the introducer of animal vaccination into this country, a man with more sterling manhood, a more honest brain, and the most comprehensive scholar it has been my fortune to meet among the physicians of this country. In fact, I will go farther, and say, that from the stand-point of a fearless manhood and a devoted and true physician, Henry A. Martin was the only whole man I have yet met in the American medical profession. He was no trimmer; no politician; in fact, he was without policy, as every man should be where truth is concerned. Most physicians in this country are trimmers. They "trim" their professional sails to suit the theological or political breeze, or social conditions. Men are so scarce! Dr. Martin spent a great deal of money trying to find a genuine case of genuine cow-pox in this country, and during his many years of earnest study found but just one. I visited some cases of eruptions in the teats of cows with him, and have been called to many others since, but in none of them has the trouble had any close resemblance to vaccina.

It is the general opinion that Jenner discovered vaccination, and it is for that that he has been honored and credited. Jenner's discovery was the humanization of vaccina; animal vaccination, true vaccination, is of much later origin, and owes more to Martin for its generalization than to any one else, but it is not the exclusive right of any one man. Jenner's method was to take vaccina from accidentally inoculated human beings, and then to pass it indefinitely from person to person. Probably the very crusts, or scabs, used on us in our youth, were direct derivatives of those first originated by Jenner.

That cows had an eruption on their teats which could be conveyed to human beings, and which did prevent small-pox in such individuals, was known long before Jenner's time, seems to be a matter beyond all question. Even that vaccination itself was practiced in England by one Benjamin Jesty, on his own wife and child, in 1774, twenty-two years before Jenner inoculated, is equally true. That vaccina in some way was transmitted to dairy people, and prevented small-pox, was also known to the common people in Germany and other parts of Europe, but no practical use was made of the knowledge. It remained for Jenner to do this. Jenner supplied the exact and trustworthy foundation to a matter of popular belief among a certain class of people, but of which the majority had no knowledge. Jenner's work was thoroughly original. There is not a particle of evidence going to show that he knew anything about the vaccination of human beings by a few others before he attempted it. Not one of those men gave any exact study to the subject, while it is said that Jenner studied, and observed, and weighed all the facts for thirty years, before he attempted to prove his observations and fortify his conclusions by direct experiment on man. This was done on a boy named Phipps, the 14th of May, 1796. But this boy was not vaccinated from a cow, but from one Sara Nilmes, who had been accidently inoculated from a cow, being a dairy-maid. The boy resisted all attempts to transfer small-pox to him by variolation.

It is doubtful if Jenner ever resorted to vaccina itself, that is, to a diseased cow, for his original material, but invariably took his stock from human beings. This should be called Jennerism, or Jennerization.

The one striking peculiarity of this and vaccination, in contradistinction to variolation, is, that the inoculated individual is not contagious to its own species. This is a very striking example of the true meaning of the word "contagion," which, as has been discussed elsewhere, seems to be entirely beyond the comprehension of the medical profession and investigators, with but very few exceptions.

Sycophantic worshippers of Robert Koch, and even the Master himself, are respectfully referred to this example, and asked to ponder a moment that they may learn that contagion and inoculability have no necessary relation, that contagion really means, that the point or locus of the primary origin of the inficiens is a diseased individual.

As has been stated, the very strongest examples of the value of vaccination are not only the very few outbreaks of small-pox which now occur, but also the almost total disappearance of cow-pox among the cattle of those people where any exact control of the question can be looked for. Statistics, as to the value of inoculation, can have but little additional importance, still, a few are appended.

TABLE SHOWING THE EFFECTS OF VACCINATION.[1]

Period of observation.		Place of observation.	Average annual death-rate from variola to the million population.	
Before vac'inat'on	After vac'inat'on		Before vaccination.	After vaccination.
1777-1806	1807-1850	Lower Austria,	2,484	340
" "	" "	Upper " and Salzburg.	1,421	501
" "	" "	Steyermark.	1,052	446
" "	" "	Illyria.	518	244
" "	1838-1850	Triest.	14,046	182
" "	1807- "	Tryat.	911	170
" "	" "	Bohemia.	2,174	215
" "	" "	Austria-Silesia.	5,812	198
" "	" "	Galicia.	1,194	676
" "	" "	Bukovina.	3,527	516
" "	1810- "	Province of East Prussia	3,321	556
1776-1780	1816- "	Poland.	1,911	743
" "	1810- "	Brandenberg.	2,181	181
" "	1816- "	Westphalia.	2,643	114
" "	" "	Rhein-Province.	908	90
1781-1805	1810- "	Berlin.	3,442	176
1780	" "	Pommerania.	1,774	130
1774-1801	" "	Sweden.	2,050	158
1751-1800	1801- "	Copenhagen.	3,128	286

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[1] Hirsch, Handbuch der Geographischen Pathologie.

The Utility of Vaccination.—"The deaths from small-pox in Germany, where there is compulsory vaccination, during the years 1887–1888, were 1.8 and 0.8 per million, respectively; while in Austria, where compulsion does not exist, the deaths were 583.7 and 540.4."—*Medical Record*, April 12, 1890.

Vaccination can be very properly termed the use of a natural method of inoculation, even though the virus is now kept up by the artificial transmission of vaccina from calf to calf. It is not the discovery of man. So far as reliable information is at hand, there is no record of the discovery and actual demonstration of the true germ of variola, though the "culture of an artificial vaccine virus, by a Russian physician, which is as effective as the genuine" vaccina, was reported in the issue of January 18, of the *Journal of the American Medical Association.* This assertion must be taken *cum grano salis*, as no mention of such a discovery seems to have been made in any of the special journals of bacteriological research. So far as my memory serves me, nothing but cocci have thus far been discovered in the eruptions of variola or vaccina. I think, when discovered, that the germ of variola will be found to be a very delicate anaërobic bacillus, and spore-bearing at that. Otherwise we cannot account for the long time which clothing, or other material, polluted by small-pox patients, retains its virulence. No non-spore-bearing organism that we now know of retains its virulence for such a length of time under such adverse nutritive conditions. I am also of the opinion that most of the endogenous germs will be found to be anaërobic.

A Few Words as to the Objections to Vaccination.—The opponents of vaccination base their opposition upon the dangers of the transmission of other diseases with which the individual may be afflicted at the time, and from whence the virus has been derived.

These objections are more applicable to the transmissions from human beings to human beings than in regard to the use of true vaccina directly. To my mind, however, they will scarcely hold water when we come to consider them critically. Take, for instance, syphilis. If, as is the case, it is at present impossible to positively isolate the germ of that disease, or even to perform auto-inoculation save from a positive syphilitic lesion; if we cannot in any way discover that germ at present—how can it be possible to transmit syphilis from an arm or locus in which there is no syphilitic lesion? It seems to me almost impossible. The same is true of tuberculosis.

The unpleasant complications following vaccination, when scabs were used, or from person to person directly, were due more to some organism which had gained access to the scab from outside, or to the carelessness of the inoculator regarding the cleanliness of his instrument, than to anything else.

The criminally careless manner in which vaccination is done even to day by too many inoculators, has already been noticed, and is absolutely unpardonable in these days of exact antisepsis and in general scrupulously clean surgery. In such a simple matter as this apparently is, many physicians appear to neglect precautions they deem absolutely necessary in their operations. And yet we even now frequently see erysipelatous or purulent complications follow. If the virus is properly collected, these things should never occur.

More precautions than are now used should be taken in the collection of the virus from calves. Why should all the points and instruments used not be completely sterilized? That they are not, goes beyond question.

The generally favorable results following the use of vaccine points by ordinarily careful physicians shows that the danger of unpleasant complications has been altogether overestimated and magnified by those opposing this valuable prophylaxis. Still, as such does exist, it seems as if some control over these matters should be exercised by law.

The danger of using diseased heifers, especially tuberculotic, need not exist, as I know from a long personal acquaintance with the senior and junior Dr. Martin, where every care is used in collecting the stock. The heifers should be collected some time in advance, and their temperature taken twice a day, and a general observation of their condition practiced. Any animal showing the least departure from normality in any direction, should be peremptorily rejected.

We will now for a moment give our attention to

Pasteurism.—The world owes an unpayable debt to Louis Pasteur, for to him is due, more than to any one else, the reopening of the field of experimental preventive inoculation, and in directions never before thought possible of offering any practical advantages. But even he has not touched upon the most important work, which is the prevention of the non-recurrent diseases of child-life, most especially scarlet fever, which is to-day the greatest scourge that threatens humanity in civilized countries. Pasteur is an explorer in an almost unknown sea of investigation. The "gates," are still but "ajar." They are not yet open. Many others are trying to enter. Some few can glance over the threshold, but the haven of success is yet a long way off.

While I do not accept the results of Pasteur's anti-rabies inoculation, I most cheerfully credit him with his earnest endeavors and the instructive value of his success in anthrax, hen-cholera and rouget in the hog. It may be well for me to state why I do not believe in Pasteur's method of preventing rabies.

1. There is not a particle of evidence to be found in the long historical record of this disease that it is non-recurrent in character. Not a single case of natural recovery in man or beast has ever been reported where the history of its origin was undoubted and the phenomena presented unquestionable. Hence, we have no natural foundation to warrant the hypothetical possibility of preventive inoculation.

2. Pasteur's statistics are not honest. Not one of those Newark children was ever bitten by a mad dog. Two were left at home, and nine or ten dogs known to have been bitten by the suspected dog were kept confined over three months. Nothing ever happened to them. While the dog was "mad" enough, it was not "rabid." It did not seek to bite any one or thing, but did bite those in its way while running. It was a case of simple frenzy from an unknown cause. Dogs are often attacked thus, without rabies having anything to do with it. Pasteur still keeps those children in his statistics, though he has been fully informed as to the true nature of the case.

3. Pasteurism in connection with rabies has become a regular mania in certain parts of Europe, especially France, and rabies or hydrophobia bears a direct relation thereto. This is easily to be seen by glancing at the statistics of rabies in Prussia, for a series of years; viz.:—

1876–7, 0; 1877–8, 6; 1878–9, 2; 1879–80, 8; 1880–1, 10; 1881–2, 6; 1882–3, 4; 1883–4, 1; 1884–5, 0; 1885–6, 2; 1886–7, 1.

All suspected or rabid dogs in Berlin are brought to the Veterinary School. This includes every dog complained of as having bitten a human being. Of this number rabies has actually resulted:

1878–9, in 5; 1879–80, 1; 1880–1, 11; 1881–2, 3; 1882–3, 1; and none since then up to June 23, 1889, when I received my report. In the whole German

Empire there were but five cases of hydrophobia reported in man, in 1886; and but four in 1887.

From 1886 to 1888, there were forty cases of hydrophobia reported in Prussia; and in 1886 and '87, only nine in all in Germany.

Now let us look at the statistics given in Pasteur's Annals.

No. persons treated.	Rabies said to have been demonstrated surely.	Diagnosed by veterinarians.	Suspected.	Total.
Dec., 1888.	45	77	20	142
Jan., 1889.	32	88	22	142
Feb., "	52	90	18	160
March, "	42	95	32	169
April, "	30	122	29	181
May, "	28	149	36	213
June, "	24	115	30	169
July, "	19	111	38	173
Aug., "	15	97	33	145
Sept., "	15	80	16	111
Oct., "	19	88	16	123
Nov., "	20	99	16	135
	341	1211	307	1853

The majority of these cases came from France and the French possessions in Algeria. Does any sane person think that there is this vast difference in the prevalence of rabies in human beings between France and Germany? If so, I am not one of them. If so, no more striking example of the inefficiency of the French Government in comparison to that of Germany in its veterinary police service and guardianship of the public health, can be found.

For three years in Nebraska I vainly tried to obtain possession of an actually rabid dog, and while a vast number of dogs were reported to have been bitten by such, not one would go rabid for me after it had been so bitten. I do not deny the disease. I simply deny its prevalence to any such degree as Pasteur's statistics seem to show. I simply do not believe them.

To show how unreflectingly even educated writers will quote such statistics, the following is taken from the TIMES AND REGISTER, of Philadelphia, April 12, 1889: "Pasteurism in Cuba.—At the Bacteriological Laboratory, in Cuba, three hundred and six persons have been treated by the 'double intensive' plan. Of these, only two died, after going through the full course; a mortality of 1.63 per cent. All these cases were bitten by dogs proved experimentally and clinically to be rabid, *or at any rate* 'suspect.' That the operations were conducted with due conservatism is indicated by the fact that only three hundred and six were inoculated out of seven hundred applicants. The opposition to Pasteur, if it still exists, has dwindled down to an infinitesimal point."

Even in these cases, not one case was known beyond question to have been bitten by an actually rabid dog, for it is admitted that "at any rate, they were 'suspects'" only. And yet the editor says: "The opposition to Pasteur, if it still exists, has dwindled down to an infinitesimal point." "Three hundred and six" persons, scared half to death on suspicion! They were "suspects" only. We can "suspect" most anything to result from treatment based on such a "suspect" foundation. The foundation of "Pasteur's Institutes" should be treated in a most "suspect" manner. They should be treated as institutions of the utmost danger to the public. Hydrophobia, or Pasteurmania, flourishes in direct proportion to their establishment.

Since my return to this country, from that sensational visit to Pasteur with the Newark boys, a very large number of such "suspects" have come to me, or have been brought to me by physicians, to obtain my opinion as to the desirability of "going to see

Pasteur." Fifty-two persons is the number I have on record, but there were a few more, notably three, since I have been in Chicago.

"Mad dogs" were very "suspect," according to the story, in each case. I talked to them calmly, ridiculed their fears, and they all left me apparently comforted. Not one went to Pasteur, and I think it can be safely asserted that no hydrophobia resulted, or I should have heard of it and the papers would have been full of it long ere this. There is a vast difference between a "mad dog" and a genuine "rabid" one. The former are frequent enough, the latter are as scarce as honest original investigators in the United States.

There is still another very strong argument against Pasteur's anti-rabidism. The germ of rabies has not been discovered. This fact in itself is not very strong negatively; but when we take into consideration that rabies is a strictly wound infectious disease in optima forma; or, perhaps better, toxic rather than septic; that, as in tetanus and many forms of surgical toxæmia, the toxic producers remain at the locus traumatica, and that the poisoning of the organism takes place from there, and goes on for some time, and that constantly during that period until a certain cumulation of such material in the nervous centers has taken place—it seems to me that the Pasteur-method is self-evidently absurd. The toxic rabies' element must be in solution (the nervous tissues being only saturated with it); and hence, though very abundant perhaps, still, not in such an excessively concentrated amount, in the small piece of cord used that it can produce the effect claimed. There is altogether too much dilution. If correct in the hypothesis that the toxic producer remains local, there can be no increase in the amount of poison introduced, save as made each day. The fact that the germ remains local indicates that in the trauma is the place to look for it, as in tetanus.

Again, where can I find record of one of Pasteur's artificially rabid dogs ever having conveyed the disease to healthy ones, as is the case in the actual disease, by biting?

These objections may seem too very finely drawn to enthusiastic worshippers of Pasteur, but it may yet be found that they have more foundation than appears on their face.

These objections to Pasteur on one point do not detract, however, from the importance of his work to the world in others, in the least. What may one really call Pasteurism? The answer to this question brings us at once to the consideration of

Artificial Preventive Inoculation, which I will discuss entirely from my own point of view, and base my remarks almost wholly upon my own work and its results. Pasteurism differs as much from Jennerism as does artificial preventive inoculation from vaccination, as practiced at present. Jennerism and vaccination consist in the inoculation of the cause of the disease to be prevented thereby, bound upon or mixed up with the products of the disease; that is, as they are found in its specific lesion at a certain period of its development.

Pasteurism, or artificial preventive inoculation, or even inoculation in the most exact sense of modern experimental etiology, is quite another thing. Instead of introducing the cause mixed up with any products of disease, we isolate it therefrom, cultivate it, and, by one of several methods found suitable, so mitigate the virulent activity of the cause, that we can inoculate without serious danger to the individual thus treated.

It has become a generally accepted fact that all infectious diseases are due to a specific cause, which belongs to some specific species of microscopic vegetable life. The scientific class to which these objects belong is the fungi, their special name being bacteria, or, in common parlance, germs. It is not necessary to go into any description of the various varieties of these germs in an article of this kind; still, it is necessary that we know a little something of the manner of action of that class in which we are momentarily especially interested.

The diseases of animals in which Pasteur has been, beyond question, successful in preventing natural infection by his method of inoculation, the names of which have already been given, and to which may be added swine plague, the yellow fever, and Texas fever in cattle, as well as typhoid fever, are all what are known as forms of septicæmia, or blood poison; the specific poison in each case being the direct result of certain unknown physiologic action on the part of the specific germ, which causes each of these diseases. All these diseases have also another attribute in common, viz.: they are extra-organismal in origin; that is, the place of primary development of the specific germ which causes each of these diseases is outside the animal organism, or in the earth or earthy material.

Though he has never to my knowledge stated it, still I think Pasteur should be credited with recognizing the fact that cow-pox was but mitigated small-pox, rendered, as has been said, non-malignant in character by successive generations of transmission from cow to cow in an accidental and unintentional manner. Pasteur endeavors to do this same thing intelligently. He but repeated the lesson thus learned in his first attempts at mitigating the action of the germs of anthrax, hen-cholera, and rouget by experimental inoculation in various species of animals, and he found that while in some species a given germ acquired even more virulence than it possessed when taken from an animal in which it had caused the natural disease, and kept on increasing in virulence for a time as he passed it from animal to animal of a certain species, still, on the other hand, the same procedure in another species of animal, carried on through a long series, not only caused the germ to lose in virulence, but after a time they acquired a certain standard of mildness, and could be safely used for inoculation.

This was imitating the results in small-pox. Pasteur went further! Such a method as the above is open to the very serious objection that, not only is an almost unlimited number of experimental animals necessary, but the expense would finally be such as to decidedly interfere with any practical benefits resulting. This led Pasteur and others to seek similar results in entirely different directions. They experimented in many ways, but the continued exposure of artificial culture of given germs to a certain degree of temperature, or their development in from two to two and one-half pressures of oxygen for a certain time, have given the best and most trustworthy results. A most singular fact came from these experiments, which was that when once a certain desired degree of mitigated virulence had been obtained by either of these methods, that cultivation of the same germs could then be carried on in the ordinary room temperature for an indefinite period, each succeeding generation retaining the same degree of mitigated virulence as the previous one and the mother culture. The result has shown that a preventive virus against anthrax, rouget, and hen-cholera has been successfully made by these investigators, by one or the other of methods mentioned.

For a very valuable account of Chauveau's experiments in mitigating the virulence of bacillus anthracis in this way, see TIMES AND REGISTER, Philadelphia, April, 1890.

Based largely upon the teachings and work of Pasteur nearly all investigators in this important field of research have been of the idea, and generally are at present, that a preventive virus can be obtained by the simple mitigation of the virulence of a germ of a naturally non-recurrent disease by artificial cultivation under certain conditions of heat, or oxygen pressure, or some other method, so that the introduction of such a culture in a given amount, produces simply a mild and non-fatal form of disease.

The practical results of inoculation, or vaccination, seem to confirm this idea. For myself, I was also of the same opinion, until it was completely shattered by most extensive experiences, and apparently positive experimental results.

It is but justice to myself to inform my colleagues, both investigators and physicians, that this business of "preventive inoculation" in swine-plague is not of my own choosing; that I am bitterly opposed to it; that I feel it is disgraceful in one being, or making any pretensions of being, a scientific investigator; that I think and know that all and every result of original research should be the property of the people; and I can truly say that, had I not the remote hope that the rewards of this distasteful business may be such as to enable me to build, equip, and plentifully endow a laboratory and hospitals for the investigation of the non-recurring diseases of child-life, where the poorest genius can have free opportunity to study and be educated, or pursue original investigations, that I would have nothing to do with it. I would not continue it for a moment, to enjoy even a handsome business income, but I hope the end desired may be attained, and that the medical profession will eventually justify the unprofessional means on account of the worth of the object attempted.

Self respect forced me to resign my position as investigator in Nebraska, on account of three years of uninterrupted intrigue, and unlimited abuse and opposition excited against me by the Agricultural Department at Washington. No other course was open to me.

This inoculation against swine-plague is a matter of more importance to the advancement of original research in this country than at first may appear to the casual observer. I can safely assert that so much success has been attained, that it can no longer be open to a single doubt. Its actual practical value can only be estimated by large and extensive experiences continued for several years. Its present value and interest is, however, mainly scientific.

Having sufficiently demonstrated that inoculation will prevent swine-plague, as Pasteur's work has been the initiative incentive to all investigations in this direction, so should this result have the same value in this country, and be a stimulus to the most energetic and exact endeavors to develop protective inoculation against other non-recurrent diseases in our live stock, but even more particularly those of our own species. If my work only succeeds in putting this stimulus in such activity that work will be inaugurated and earnestly continued, and lead to the establishment of National and State laboratories, all that I have labored for will be attained, and my life be pronounced a success. My interest is far more in inspiring and inaugurating true original research in this country, than in my personal success as an investigator. If the last can only lead to the first then I am satisfied.

In this paper I unfortunately can only place before the world my failures, as in justice to my financial supporter I cannot publish the methods by which I have obtained success, much as it is my desire to, but something valuable can, I hope, be learned from my failures.

As has been said, I began the search for preventive inoculation in swine-plague on the principle of mitigation of virulence, so as to obtain a virus that would not seriously disturb the hogs, and yet render them immune from disease.

At this time and place I will simply reassert that this has been done, and in so many places and in so many hundreds of animals, that the fact is beyond the possibility of doubt.

From this non-virulent point of view the first desideratum is to obtain a virus, or culture, of a constant degree of mild virulence. As inferred above, various methods have been empirically discovered. Pasteur, as has been seen, used certain forms of animal life at first, carrying the virus from one to another of a given species in which it slowly lost in virulence until it acquired a desired benignity. He also found that an augmentation of virulence, until it acquired an equal constance in malignity, could be produced in some other species of animals. This was too expensive a method to be practiced. He then found that the exposure of the cultures to a certain degree of heat for a certain time would also produce the desired mitigation. Others have proven these observations to be trustworthy. Chauveau works by the oxygen pressure method, and has obtained the same result. We need not discuss others.

The great fact is that once the desired degree of mitigation has been obtained in any virus, that the virus thus obtained can be then cultivated in ordinary media (fluid) outside of those conditions, and that the virus thus obtained will retain this constant degree of mitigated virulence for a long time. If a spore-bearing germ, this condition may be retained almost indefinitely, but in non-spore-bearing organisms it is not so reliably constant. The first thing, then, was to obtain a constancy of virulence in the desired direction.

I have never thought that either of the above methods was strictly scientific. They are too artificial; hence, as far as swine-plague is concerned, I have endeavored to produce the same result by a more natural procedure. That is, by chemical nutrition, for this virulence is entirely a physiological-chemical result, and absolutely dependent upon the nutritive qualities of the media in which germs develop. It has been said that, once a desired degree of mitigation was arrived at, it could be retained in artificial cultures for an indefinite period.

With regard to the swine-plague germ, other investigators have not only declared this to be impossible, but also unnecessary. I shall show that it can be successfully done, but cannot, unfortunately, tell how, for reasons previously given. I think I shall also be able to show that, in a certain sense, no great result has been obtained when we have done it.

Attention has been called to the fact that others could not obtain this constancy in mitigated virulence, and, furthermore, that it was unnecessary in swine-plague.

In a paper on "Hog-Cholera," which is the disease I call "Swine-Plague," one of these diletants says: "I shall not go into the details of preventive measures in this paper. * * * What you are doubtless interested in, is the new points which may have been brought out by our investigations. The most interesting of these is our attempt to confer immunity by inoculation. We soon found that there was no indication for attenuating the virus for this purpose, because the strongest virus might be introduced hypodermically, with impunity, in considerable doses. Now, as the stronger a virus is, the higher the degree of immunity it produces, you can see that there is every reason for using fresh unattenuated cultures. We made many experiments, and found that hogs might safely be inoculated with one-quarter to one-half a ccm. for the first dose, and that the second dose might be safely increased to two to three ccms., showing that some degree of immunity had been gained. Those twice inoculated, however, were still unable to stand exposure in an infected pen, and could not be fed the virus without fatal results."—*Journal of Comparative Medicine.* Philadelphia, Pa., April, 1888, Vol. IX, p. 149.

Let us consider these statements a little. First, not only their general tenor, but that of all the subsequent publications of the same author, show, according to him, that swine-plague cannot be prevented by inoculation. It is interesting to read, in this connection, what the same authority said in 1883, five years previous to the above, when, as can be shown, he had no idea what the germ of swine-plague was; but, supporting himself on the authority of Pasteur, he asserted a micro-coccus to be that cause. Swine-plague was not discovered in France until 1887.

He said: "Our investigations have shown that the plague is a non-recurrent fever, and that the germs might be cultivated; they have even proved that these germs may be made to lose their virulent qualities and produce a mild infection. Surely we have here sufficient evidence to show that a reliable vaccine might be easily prepared if we carried our investigation but a little way farther.

"Mr. Pasteur has recently confirmed (?) our American investigations in a very complete manner. He shows that the disease is produced by a micro-coccus; that it is non-recurrent; that the virus may be attenuated, and protected from subsequent attacks, and he promises a vaccine by spring."—Report Department of Agriculture. 1883, page 57.

That the above was made out of whole cloth is shown by the following:

First. A micro-coccus is not the cause of swine-plague.

Second. The government knew of only one swine-plague until 1886, and a coccus is not the cause of either hog-cholera, or the nondescript disease it now calls swine-plague.

Third. Pasteur studied "rouget," and not swine-plague.

Fourth. A bacillus has been proven to be the cause of "rouget," and not a micro-coccus.

Fifth. Pasteur's virus against rouget does prevent.

Sixth. If in 1883, this person said: "Surely we had sufficient evidence to show that a reliable virus might be easily prepared," what has become of that evidence since then? It is singular that my success in preventive inoculation should dispel it as easily as the morning sun does the fog of the prairie.

As to preventive inoculation in swine-plague I will quote the following only from my address before the Live-Stock Breeders' Association, of Nebraska, February last:

"My only sin has been that I forestalled the ambition of the government, which being one 'for the people,' we might suppose would be an act to receive kind endorsement rather than the most bitter and fanatical opposition.

"Even that 'Board of Inquiry' admitted that inoculated hogs stood the tests they were exposed to better than hogs which had recovered from a natural outbreak.

"Professor Burrill, in a moment of unprejudiced honesty, wrote me that 'none stood the tests so well as the Nebraska hogs.'

"With these facts publicly announced to those most and directly interested, a political neophyte, in a recent publication, claims that he has a letter from the president of that 'Board of Inquiry,' Dr. Shakespeare, in which the latter says that the Nebraska hogs were equally sick, when put in a diseased herd, with a lot of healthy ones also put in the same herd. Then why did not Dr. Shakespeare tell the farmers that in the published report?

"Was it not the sacred duty which he owed to science and to every hog raiser in this country?

"On the contrary, that part of the report to which he had his name attached says, without any reservation whatever, that the Nebraska hogs stood the tests better than those naturally recovered.

"What more then, can you ask?

"Does not that assertion of Dr. Shakespeare's, indorsed by Prof. Burrill's signature, and by his later letter, not only emphasize and confirm the reiterated statement of the government, that the disease is 'non-recurrent?'

"If the inoculated hogs stood the tests better than recovered hogs from a naturally 'non-recurrence' disease, then art beats nature, and inoculation has proven to be a reliable fact, one established beyond question, no matter if an occasional failure does occur, as it has in my practice since I left you, and since I have had to entrust the business to other hands, and, from the very opposition of the government, resort to an undue precaution, which, had I remained here, would never have been necessary."

To the above I add one testimonial from a practical farmer, contributed to the *Breeder's Gazette*, of April 2, 1890:

"Mr. R. C. Fulton, Taylorville, Ill., writes: 'The reports in your issue of March 19, by C. A. Cantine, A. R. Hubbard, Marion Ryman, on inoculation, remind me that it is surely due Dr. F. S. Billings, also the farming world, that I should make report of my experience with two inoculated boars sent me for the purpose of proving, so far as possible, that inoculation is a preventive. The pair of hogs were received about February 8, and at once placed in the lot of about one acre, adjoining which were breeding pens for six sows. In the lot and pens named I had lost forty head of hogs, and yet had a few left when the boars were placed in pens. These hogs have continuously bedded on the same litter, and in the same pen where eight had laid while sick and dying. I have them fed on ear corn only, and that was strewn on the excrement and cleanings from other infected pens, and for drink they have had slough water, which catches the waste of barn, lot and pens above named. This I consider a crucial test, and I felt nothing short of that would satisfy even my unprejudiced mind as to the prevention of swine-plague by inoculation. Many of my neighbors have looked on incredulously, and I was even laughed at by my more verdant ones; but the laugh ceased; incredulity has vanished, and all admit that something prevented, and what else but inoculation? For my herds have been reduced or swept away before. In conclusion, the hogs named are doing fine on the same ground where forty died.'"

Scientifically speaking, this is sufficient evidence to prove the fact.

Now, as to that irresponsible statement that "we soon found that there was no indication for attenuating the virus, because the strongest virus might be induced with impunity in considerable doses."

Whether one ccm. is to be looked upon as a "considerable dose" or not I will not attempt to decide, but that I can select an outbreak of swine-plague from which that dose, in the first generation of cultivation, will produce fatal effects, as well as that inoculation will prevent, is shown by the following:

In December, 1888, I desired to test a number of inoculated hogs for a special purpose. At the State Penitentiary there raged one of the most malignant outbreaks on record. By malignant I mean acutely fatal, not prolonged, and still fatal in its course. From one of these hogs I obtained a culture and inoculated, in the flank, seventeen healthy uninoculated hogs, and twenty inoculated ones, with one ccm. of the first culture, Fifteen of the uninoculated pigs died, and all were sick. The others were not affected at all. Cultures from the original penitentiary hog, and from several of those which died, with full autopsy notes, were sent to Professor Welch, of Johns Hopkins.

This, then, shows that "considerable doses" of the strongest virus cannot be used with impunity, and also that immunity can be produced by mitigated cultures, as none of the inoculated hogs were made seriously ill during their treatment.

The germ of swine-plague varies very much in acuteness of virulence, as every one knows, and this is shown in nearly every outbreak one studies. Rabbits have been considered to be suitable animals to control this point, of which one observer says: "Rabbits die from hog-cholera inoculations in six to nine days."—*Journal Com. Med.*, e. c., p. 133. On this point Welch says: "The duration of life after inoculation of rabbits is usually from five to fourteen days, and it may be even longer."—*Journal Com. Med.*, Vol. I, 1890, p. 52. "Rabbits when inoculated die usually in six to eight days."—*Bulletin*, *Johns Hopkins University*, December, 1889.

In an attack upon preventive inoculation, made by a tool of the government before the Kansas Board of Agriculture, we find the following interesting passages:

1. "Prevention by inoculation depends upon the well-known principle that one attack of a contagious disease generally protects the individual from the subsequent attacks of that contagion. All individuals, however, are not protected in this way from any disease, and in many cases the protection only lasts for a short period."

Comment is unnecessary.

2. "The dose is not the only factor which must be considered when inoculating. The strength of the virus varies in different outbreaks of the disease so much that the dose, which would be perfectly harmless in one case, would be as certainly fatal in another. As there is no reliable test of the strength of virus, but experiments upon hogs, and as the strength varies during artificial cultivation, you will see that it is next to impossible to accurately know the strength of the virus he (Billings) is using."

3. "Inoculation in practice consists in injecting under the skin as much of the strong virus of hog-cholera as can be safely given without producing a fatal type of disease. It must be remembered that inoculation is very different from vaccination. The virus used in inoculation is the same as is found in hogs dying of the plague, while in vaccination a virus is used so weakened that it cannot cause a fatal disease. No method of vaccination has yet been introduced for hog cholera. It is inoculation that is being advertised as a preventive for hog-cholera, and it is a question of the size of the dose whether the disturbance produced in the hog's body is mild or fatal in character."

From all that has been quoted from these authorities it is evident that they have no idea of a constancy of virulence in the swine-plague bacilli, or that such can be obtained.

It has already been stated that in Pasteur's and other methods of mitigation, when a certain desired degree of mitigated virulence had been once obtained, cultures of the same degree could be then carried on for an indefinite period.

This led me to the study of the following questions:

1. Is there a mitigated or non-fatal degree of virulence to be found in natural outbreaks? or, in other words, can a vaccine virus be at once obtained from a natural outbreak? This I proved to be an unquestionable fact, easy of demonstration at any time, though it took much study and very close observation of the relation of certain pathological lesions to the desired degree of virulence to obtain the knowledge, and some experimentation to prove it.

2. Can this or any natural degree of virulence be retained indefinitely by any method of artificial cultivation by nutritive measures alone?

3. Can this micro-organism be fed up and down in virulence by changes in nutrition alone?

4. Can a direct proportional relation be established between a certain dose of virus of known virulence in small animals and a safe or preventive dose of the same virus in hogs?

The three last questions have all been solved in a most exact and satisfactory manner.

It is possible for me to almost invariably select an outbreak of swine-plague from which a given dose of the first cultivation will kill a rabbit on subcutaneous inoculation in approximately four days, and, by a very slight variation in nutrition, to bring and retain such a virus to this point of virulence in a very few generations.

In order to demonstrate this point, I will give the result with several viruses:

VIRUS NO. 1.			VIRUS NO. 2. †		
Generation.	Date of inoculation.	Killing time, days.	Generation.	Date of inoculation,	Killing time, days.
1	Sep.28 1888.	4	1	Sep.28, 1888.	4
35	Jan. 5, 1889.	4	77	Oct. 5, 1889.	4
76	Oct. 2, "	5	78	" 13, "	3½
78	" 16, "	4	79	" 16, "	4
79	" 23, "	4	80	" 23, "	3¼
80	" 30, "	3½	81	" 30, "	3½
81	Nov.10, "	4	82	Nov.10, "	3½
82	" 17, "	3½	83	" 17, "	3½
83	" 25, "	4	84	" 25, "	3⅛
84	Dec. 2, "	4	85	Dec 4, "	5
85	" 9, "	4	86	" 11, "	3¾
90	Jan.26, 1890.	4	90	Jan. 10,1890.	3¾
93	Feb.22, "	3½	95	Feb.22, "	3½
95	Mar. 9, "	2¾			
98	" 31, "	6*			
99	Apr. 6, "	4			
100	" 13, "	4			
101	" 20, "	4			

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* This rabbit had survived a very delicate inoculation, made on 16th of March.

† From an outbreak on another farm.

VIRUS NO. 3.			VIRUS NO. 4.		
Generation.	Date of inoculation.	Killing time, days.	Generation.	Date of inoculation.	Killing time, days.
1	Oct. 2, 1889.	4½	1	Oct. 3, 1889.	3
2	" 9, "	3	2	" 9, "	4
3	" 16, "	3	3	" 16, "	4
4	" 23, "	4	4	" 23, "	4
5	" 30, "	4	5	" 30, "	3½
6	Nov.10, "	3½	6	Nov.10, "	4
7	" 17, "	3½	7	" 17, "	3
8	" 25, "	4	12	Dec. 24, "	3¾
9	Dec. 4, "	3¾	13	Jan. 1, 1890.	3¾
10	" 11, "	3½	16	" 26, "	3¾
11	" 18, "	3½	20	Mar. 2, "	3½
15	Jan.19, 1890.	3⅛	21	" 9, "	3
19	Feb.22, "	3½	24	" 31, "	3¾

VIRUS NO. 5.			VIRUS NO. 6.		
Generation.	Date of inoculation.	Killing time, days.	Generation.	Date of inoculation.	Killing time, days.
1	Dec. 19, 1889.	2½	1	Jan 30, 1890.	2¾
2	" 24, "	2½	2	Feb. 2, "	2½
3	Jan, 1, 1890.	4	4	" 22, "	3½
4	" 10, "	4	6	Mar. 9, "	4
5	" 19, "	4	9	" 31, "	4
6	" 26, "	4	10	Apr. 6, "	4
8	Feb. 22, "	3½	11	" 13, "	4
13	Mar. 31, "	4½			

From the first generation of this virus No. 5, seven healthy hogs received one cubic centimeter in the inside of the thigh subcutaneously; two of these died, which were closely confined, within ten days; the others were at first loosely confined, and showed no ill effects; but after the fifteenth day they were changed to the closest confinement possible, and all died between the thirtieth and thirty-fifth days; while five others, which were given plenty of room to roam about, and which received the same dose, all lived. This experiment was made to demonstrate, if possible, a certain well-known fact of practical experience.

It has always been told me that if such hogs were shipped, that the death-rate would be checked, or even stopped, while on the cars; and it has also become more or less current among farmers that to put sick hogs on a wagon and rattle them over frozen and rough ground was a good thing to do. In some few cases evil results have followed inoculation. Some few hogs have either died after a prolonged illness or become somewhat stunted; while others, inoculated with the same dose of the same virus, have shown no ill effect. It therefore becomes an interesting question to discover why this should occur in one case, and not in a great many others.

After very careful inquiry it was discovered that, where ill effects followed inoculation, the animals were kept very closely confined, and had not room enough to move around, and that this was the cause; or, in other words, insufficient movement to stimulate the circulation. A very striking example of this occurred in two bunches of hogs inoculated at the same time for a gentleman who is a personal friend and a great advocate of inoculation. At his house were twenty-five hogs in a small pen, while in a field, running with his cattle, were about one hundred and twenty-five others. Those in the small pen had a prolonged and very severe attack of swine-plague in consequence of the inoculation, though none died; while the one hundred and twenty-five in the field showed no ill effects whatever.

Exactly the same thing occurs in typhoid fever in man. The patient has recovered from his typhoid, and the physician congratulates him; the next day he is cyanotic, rapid breathing is present, and pneumonia develops: owing to stagnation of the circulation, and the reflow, or pressure, of the blood to the point of least resistance, which is the lungs.

The above tables show that a standard of virulent activity can be produced in cultivations of the swine-plague germs simply by proper nutrition. They further show that not only the selection of material from a natural outbreak can at once provide a preventive virus; but also that, in successive cultivations for generations, this standard can be retained at a greater degree of virulence than other observers claim to have found in natural outbreaks by their controls in rabbits.

Now I must positively, and against every and any assertion to the contrary, assert that I can prevent swine-plague by inoculation. Were I not bound as

I am, I would give records of other viruses possessing no virulence whatever, which have produced and still produce an absolutely immune condition in nearly every hog inoculated.

To discover this fact has cost an immense amount of experimentation and a large amount of money. There is one difficulty about it which cannot be overcome. While the virulence of a culture can accurately be tested on small animals, and the exact relation be established between that virulence and a safe dose in the animals in which a given non-recurrent disease occurs naturally, we have no means of testing the preventive properties of a virus, except the results in inoculated animals of the species in which the disease naturally occurs, and this takes a long time and a great many inoculations.

When I began this work, I thought that a test of virulence, with a proper regulation of the proportional dose, was all that was necessary; now I know that a test of virulence with such proportional control is of no value whatever with reference to the protecting power of a given virus. I know this by an experience in over one thousand five hundred hogs. Either one of the six viruses named above will kill a hog by subcutaneous inoculation in sufficient doses, but more reliably by feeding experiments; yet not a single one of them will protect a hog an iota against the cholera; while a germ virus, without any virulence whatever, even by forced feeding, will protect securely and almost invariably, in single doses of one cubic centimeter.

This assertion is obviously contradictory to all previous experiences, and yet, if one stops to think a moment, supported by the most trustworthy experience which we have.

There is no question that, under certain circumstances, using a natural virus, we must reduce the virulence to a certain degree in order to produce a fatal attack by inoculation; but, on the other side, we do not need to have a virus possessing any virulence whatever to produce immunity in a non-recurrent disease.

Vaccination gives the best possible example of the point we desire to call attention to. While in variolation small-pox itself was transmitted, and the variolated person was as much a source of contagion as one having the natural small-pox, the vaccinated individual is absolutely non-dangerous to those coming in relation therewith.

What has been lost?

Certainly something; and the practical evidence conclusively demonstrates that it must have been, or is, that peculiar element of the germ, the contagion, which rendered the variolated person dangerous while the vaccinated one is not.

It is a question of nutrition only, which can be demonstrated by exact experimentation if we only try.

The bovine organism must offer certain nutritive conditions which, in some unknown way, rob the micro-organismal cause of small-pox of its contagious (small-pox) producing qualities, while the preventive one is retained in optima forma.

The same thing can be done with the germ of swine-plague, but to no such degree of absolute certainty as nature or accident has accomplished in vaccina. While it is the easiest possible matter to feed the germ of swine-plague up and down in virulence, to make it extra malignant, or rob it of that quality altogether by changes in the chemical nutrient, it is a most difficult thing to retain the preventive physiological qualities of these germs. Sometimes it can be done for months, and again they are lost in a few generations; but we have no control over these [illegible] cept the practical tests. None of the small animals which I have tried can be easily or successfully rendered immune against swine-plague. Rabbits and guinea-pigs can be rendered somewhat immune by repeated inoculations of small quantities of virus; but, so far, I have been unable to render them absolutely so. Pigeons vary; but no more artificial immunity can be produced in them than they naturally have, as will be shown later, and at another time.

As has been repeatedly mentioned, a test or control of virulence has nothing whatever to do with the protective power of a virus. It simply shows that it is safe to use, and that we can establish the point of safety by experiment.

This shows that we have all been working on an erroneous basis. Prevention has no relation to specific virulence. Others have demonstrated the same fact.

In THE TIMES AND REGISTER, Philadelphia, of April 12 and 19, were published a series of most interesting experiments by Chauveau, the most eminent and conservative experimenter in France, in which he demonstrates it in connection with bacillus anthracis. Chauveau says,[1] that "Energetic vaccinal (preventive) properties have been discovered in a pathogenic germ (B. anthracis) not only attenuated in its virulence, but systematically deprived of all infectious properties—rendered so neutral and inactive that we were forced to ask ourselves if this transformed microbe had not become a new species."

"Cultures of bacillus anthracis in this condition can then be carried on in the ordinary atmosphere."

Chauveau conclusively shows that bacillus anthracis produces two chemical elements in its bio-physiological development; the one toxic, or specifically disease-producing, the other having exclusively preventive properties; and that, by cultivation in two to two and one-half pressures of oxygen, the toxic properties may be, or are, lost, while the preventive are retained. Or, to use his own words, "In fact, in my experiments the vaccine property of the transformed bacillus anthracis is so active, and so well survives the loss of all infectious properties, that we seem authorized to consider these two properties as being absolutely independent of each other, and as each belonging to a special product of microbe life."

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[1] The original appeared in *Archives Med. Experimentale*, March, 1889.

Another point in evidence of this fact is this: if we take a culture of the germ of swine-plague which has experimentally been shown to actively possess both of these preventive and toxic, or disease-producing, qualities, by actual experimentation, and freeze it solidly for several days, and then inoculate or feed hogs with it, we will find that, while it has retained its toxic, or disease-producing, properties without mitigation, it has entirely lost its preventive property.

That bacillus anthracis has the power of producing these two essentially different chemical elements has also been well shown by Heuppe and Wood.

Though I sometimes criticise the conclusions of my friend Hueppe, still I think him one of the most competent and reliable patho-bacteriologists living, especially in regard to physiologico-chemical attributes of pathogenic bacteria. In the publication mentioned Hueppe and Wood describe a saprophytic bacillus absolutely without virulent qualities, which, in every method of artificial cultivation, or under the microscope, bore such close resemblance to B. anthracis that it could not be distinguished from that organism. It is a well-known fact that all previous experimenters had not been able to render mice immune to anthrax by n of preventive inoculation; and yet, with this absolutely non-virulent germ, Heuppe and Wood were successful in rendering these most susceptible animals immune to extremely virulent cultures of bacillus anthracis.

Now, it is neither logical nor reasonable to suppose that this was any other micro-organism than bacillus anthracis. It was derived from the earth possessing exactly the attributes described by these observers. In this case the nutritive conditions in the earth had naturally produced exactly the same physiological-chemical conditions in bacillus anthracis which Chauveau has conclusively demonstrated to be possible of production by the cultivation of the same germ under certain degrees of oxygen pressure, and I have been able to do with the swine-plague germ by chemical nutrition, the only difference being that while I have, as it were, "gone it blind," not being a chemist, and accidentally hit on a means of arriving at a certain practical result by innumerable changes in chemical nutrition, until I have empirically arrived at a method of obtaining a certain result for an uncertain length of time, Chauveau has found a definite means of obtaining it with reference to the bacillus anthracis.

That the chemical nutrition method is the one by which practical results will eventually be obtained goes without question; but it remains for the chemist alone to really discover and perfect it.

The discovery of Hueppe and Wood regarding bacillus anthracis finds its confirmation in many diseases of extra-organismal origin, and explains that heretofore mysterious condition known as "acclimatization" in diseases of this character: such as yellow fever, Southern cattle plague, etc. In these cases the specific germs, in a saprophytic or non-malignant condition, must have gained entrance to the individuals possessing this acclimatization immunity while they possessed this prophylactic power, though not possessing the toxic or disease producing.

That all these exogenous germs are, or can be, changed to saprophytic must be self-evident; and that their toxic or disease-producing property is acquired by peculiar nutritive conditions in the soil which they naturally inhabit seems also equally clear. In fact, their acquisition of disease-producing qualities is dependent upon the prolonged saturation of the ground with the excreta of animal life or the decayed products of animal tissues. The delicacy of the action of these germs in different nutritive media is so little understood, and has enjoyed so little experimentation, especially chemical investigation, that we really know very little about it; yet it is the open field of original research which will eventually lead to success, and from which we can only hope for decidedly practical results.

Why the swine plague virus should lose its virulent properties in cattle, or even when cultivated in sterilized cattle urine, is a question no one can decide at present. Why the germ of the corn-fodder disease should not be toxic to animals while still manifesting its presence by specific lesions in green and growing corn, and only become toxic when and after the leaves begin to wither and the chlorophyl suffers chemical changes, are also questions of a nutritive nature which can only be elucidated by the most exact chemical investigations.

At one time in their existence all these organisms are saprophytic, and again they become pathogenically toxic, all of which is determined by the material they develop in.

Before closing, I desire to say a word in relation to fluid-cultivating media. When the study of bacteriology first began, these were the only media we had, and it was next to impossible to obtain perfectly pure cultures for the want of a reliable means of isolation. Koch supplied us with this means, but, in doing so, led to an altogether too great neglect of fluid media, which has retarded investigation to a degree not sufficiently estimated by the majority of investigators.

Once it was thought that the only way by which pure cultures could be legitimately attained was by the isolation method offered by the solid media on plates, according to Koch. Now we know that, in the majority of cases, if we inoculate a susceptible animal with material containing a variety of micro-organism derived from an animal having a specific disease, in general, the germ of the latter only will develop; and that, from the specific lesions, we can generally obtain the specific germ in a pure condition if we take the necessary precautions. It is singular that the lesson of this experimental experience has not made more of an impression upon investigators. Why is not the same rule applicable to animals or individuals afflicted with the natural diseases? In other words, why not pathologically decide which is the specific lesion in a given disease, and by experience discover the period in which it is truly specific, and then make cultures directly from it at that time? This point decided, pure fluid cultures can be almost as easily and surely obtained in septicæmic diseases as by recourse to solid media.

In swine-plague, Southern cattle-plague, and the cornstalk disease, all septicæmic in character, I have invariably used fluid cultures in connection with the solid, and with equally successful results as to purity.

The virus No. 1, to which attention has been called, is now in its one hundred and second generation: that is, it has been carried on successfully through about one hundred fluid cultures without one single pollution occurring during all that time. We must resort to fluid cultures if we will be successful in preventive inoculation, for this procedure is one, as well as virulent inoculation, which depends entirely upon the chemical food offered, and only with fluid media can we experiment in that direction or prepare the way for the chemist. Germs which soon lose their virulence on or in solid media retain the same indefinitely in appropriate fluid cultures. Starting with a pure culture, there is no more danger of pollution in the transference from fluid media to the same than in solid media, if one is rapid and dexterous in his manipulations. It is simply a question of strict sterilization and rapid dexterity which gives satisfactory results in either case.

Let me again say that it is only from nutritive experimentation with chemical fluid media that we can arrive at any satisfactory results.

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